

U.S.S.N. 10/012,202

Filed: December 5, 2001

## AMENDMENT AND RESPONSE TO OFFICE ACTION

## In the claims

1. (original) A biphasic antihistamine composition in daily oral uni-dosage or divided dosage form which comprises:
  - (a) a therapeutically effective amount of a sedating antihistamine to inhibit histamine release for a duration of about 4 to 12 hours, and
  - (b) a therapeutically effective amount of non-sedating antihistamine to inhibit histamine release for a duration of 10 to 20 hours, with a delayed release 6 to 10 hours after ingestion.
2. (original) The antihistamine composition defined in claim 1 wherein the sedating antihistamine is selected from the group consisting of brompheniramine, chlorpheniramine, debrompheniramine, dexchlorpheniramine, carbinoxamine, clemastine, diphenhydramine, pyrilamine, tripeleminamine, triprolidine, methdilazine, bromodiphenhydramine, promethazine, azatadine, cyproheptadine, diphenylpyraline, doxylamine, trimeprazine, phenindamine, ketotifen, hydroxyzine, tazifylline, temelastine, meclizine, acrivastine, setastine, oxatomide, mequitazine, levocabastine, lodoxamide, AHR 11325, phenindamine, azelastine, and ebastine, or a pharmaceutically acceptable salt thereof.
3. (original) The antihistamine composition defined in claim 1 wherein the non-sedating antihistamine is selected from the group consisting of fexofenadine, loratadine, descarboethoxy loratadine, astemizole, norastemizole, desmethylastemizole, cetirizine, acrivastine, and temelastine, or a pharmaceutically acceptable salt thereof.
4. (original) The antihistamine composition defined in claim 1 wherein the sedating antihistamine has a duration of activity of about 6 to 10 hours.

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5. (original) The antihistamine composition defined in claim 1 wherein the non-sedating antihistamine has a duration of activity of about 12 to 18 hours.
6. (original) The antihistamine composition defined in claim 1 wherein the sedating antihistamine is releasable immediately or up to 1 hour following administration.
7. (original) The antihistamine composition defined in claim 1 wherein the non-sedating antihistamine is releasable immediately or up to 1 hour following administration.
8. (original) The antihistamine composition defined in claim 1 which further comprises a therapeutically effective amount of at least one agent selected from the group consisting of an analgesic agent, an antitussive agent, an expectorant, an anti-inflammatory agent, an anti-pyretic agent and a decongestant.
9. (original) A method of inhibiting the release of histamine in a patient which comprises the step of administering to the patient, a therapeutically effective amount of the antihistamine composition defined in claim 1.
10. (original) The method of inhibiting the release of histamine defined in claim 9 wherein the antihistamine composition is administered during the evening or night and the sedating antihistamine is immediately released.
11. (original) The method of inhibiting the release of histamine defined in claim 9 wherein the antihistamine composition is administered during the evening or night and the non-sedating antihistamine is released the next day, 6 to 10 hours following administration.
12. (original) The method of inhibiting the release of histamine defined in claim 9 wherein the patient suffers from allergic reaction, allergic rhinitis, cold or flu.

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13. (original) A biphasic antihistamine composition in daily oral uni-dosage or divided dosage form which comprises:

(a) a therapeutically effective amount of a non-sedating antihistamine to inhibit histamine release for a duration of about 10 to 20 hours, and

(b) a therapeutically effective amount of sedating antihistamine to inhibit histamine release for a duration of 4 to 12 hours, with a delayed release, 8 to 12 hours after ingestion.

14. (original) The antihistamine composition defined in claim 13 wherein the non-sedating antihistamine is selected from the group consisting of fexofenadine, loratadine, descarboethoxy loratadine, astemizole, norastemizole, desmethylastemizole, cetirizine, acrivastine, and temelastine, or a pharmaceutically acceptable salt thereof.

15. (original) The antihistamine composition defined in claim 13 wherein the sedating antihistamine is selected from the group consisting of brompheniramine, chlorpheniramine, debrompheniramine, dexchlorpheniramine, carbinoxamine, clemastine, diphenhydramine, pyrilamine, tripeleminamine, triprolidine, methdilazine, bromodiphenhydramine, promethazine, azatadine, cyproheptadine, diphenylpyraline, doxylamine, trimeprazine, phenindamine, ketotifen, hydroxyzine, tazifylline, temelastine, meclizine, acrivastine, setastine, oxatomide, mequitazine, levocabastine, lodoxamide, AHR 11325, phenindamine, azelastine, and ebastine, or a pharmaceutically acceptable salt thereof.

16. (original) The antihistamine composition defined in claim 13 wherein the non-sedating antihistamine has a duration of activity of about 12 to 18 hours.

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17. (original) The antihistamine composition defined in claim 13 wherein the sedating antihistamine has a duration of activity of about 6 to 10 hours.

18. (original) The antihistamine composition defined in claim 13 wherein the non-sedating antihistamine is releasable immediately or up to 1 hour following administration.

19. (original) The antihistamine composition defined in claim 13 which further comprises at least one agent selected from the group consisting of an analgesic agent, an antitussive agent, an expectorant, an anti-inflammatory agent, an anti-pyretic agent and a decongestant.

20. (original) A method of inhibiting the release of histamine in a patient which comprises the step of administering to the patient, a therapeutically effective amount of the antihistamine composition defined in claim 13.

21. (original) The method of inhibiting the release of histamine defined in claim 20 wherein the antihistamine composition is administered during the day and the non-sedating antihistamine is immediately released.

22. (original) The method of inhibiting the release of histamine defined in claim 20 wherein the antihistamine composition is administered during the day and the sedating antihistamine is released in the evening or night, 8 to 12 hours following administration.

23. (original) The method of inhibiting the release of histamine defined in claim 20 wherein the patient suffers from allergic reaction, allergic rhinitis, cold or flu.

24. (original) The antihistamine composition defined in claim 1 wherein the delayed release portion is achieved by coating a core or granulations with at least one delayed release control polymer selected from the group consisting of ethyl cellulose,

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cellulose acetate, cellulose acetate phthalate, hydroxypropyl methylcellulose phthalate, polyvinyl acetate phthalate, acrylic acid polymers and copolymers, polymers or copolymers of methacrylic acid, methyl acrylate, ethyl acrylate, methyl methacrylate, ethyl methacrylate, hydroxypropyl methylcellulose acetate succinate, shellac, cellulose acetate trimellitate, vinyl acetate, azo polymers, pectin, chitosan, amylose, guar gum, and zein or combination thereof.

25. (original) The antihistamine composition defined in claim 8 wherein the analgesic agent, antitussive agent, expectorant, anti-inflammatory agent or decongestant is in a sustained release form.

26. (original) The antihistamine composition defined in claim 25 wherein the sustained release effect is achieved by formulating the analgesic agent, antitussive agent, expectorant, anti-inflammatory agent or decongestant with a sustained-release control polymer selected from the group consisting of methyl cellulose, ethyl cellulose, wax, gums, cellulose acetate, cellulose acetate phthalate, hydroxypropylmethylcellulose succinate, polyvinyl acetate phthalate, acrylic acid polymers and copolymers, polymers or copolymers of methacrylic acid, methyl acrylate, ethyl acrylate, methyl methacrylate, ethyl methacrylate, hydroxypropyl methylcellulose acetate succinate, shellac, cellulose acetate trimellitate, vinyl acetate and combination thereof.

27. (original) The antihistamine composition defined in claim 13 wherein the delayed release portion is achieved by coating a core or granulations with at least one delayed release control polymer selected from the group consisting of ethyl cellulose, cellulose acetate, cellulose acetate phthalate, hydroxypropyl methylcellulose phthalate, polyvinyl acetate phthalate, acrylic acid polymers and copolymers, polymers or

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